








## Research paper

# Cardiac function in TTTS twins after laser coagulation



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## Abstract

**Introduction:** Cardiac function in twin pregnancies complicated by twin-to-twin transfusion syndrome (TTTS) is an important issue in order to understand the modifications that any intervention aimed to solve the blood transfusion can determine on the surviving fetuses. Many studies have shown that in the long term, after laser coagulation (LC) of severe TTTS syndrome, cardiac function and blood pressure return to normal in the majority of surviving twins. This indicates that the preceding cardiac dysfunction regresses once LC has removed the underlying cause. However, a reported increased in the prevalence of pulmonary stenosis despite successful LC justifies the need for prenatal and postnatal cardiac surveillance.

**Material and methods:** In our data of 28 pairs of twins complicated by TTTS and undergoing LC, we observed abnormal prenatal cardiac findings before treatment and the postnatal occurrence of some structural heart defects. One twin recipient with hydrops and functional pulmonary atresia had the same features at postnatal follow-up; another twin recipient with fetal hydrops, and mitral and tricuspid valve regurgitation presented with moderate pulmonary stenosis postnatally.

**Results:** One fifth of all TTTS recipient twins show congenital and/or acquired diseases, i.e. right ventricle outflow tract obstruction (RVOTO), PA, or PS. Laser coagulation in severe stages can solve the blood transfusion but does not solve the acquired CHD (such as right ventricular outflow obstruction and pulmonary valve atresia).

**Conclusions:** Laser coagulation should always be performed before cardiac function deteriorates, if possible.

**Key words:** laser coagulation, TTTS, RVOTO, pulmonary atresia, pulmonary stenosis, twins.

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## Introduction

In recent years multiple pregnancies have increased globally, in keeping with lifestyle changes, an increase in maternal age, and the use of assisted reproductive techniques (ART). However, multiple pregnancies contribute

disproportionately to prematurity and perinatal mortality and morbidity [1].

Whereas in the past multiple pregnancies often went undiagnosed until delivery, today improved antenatal management, including ultrasound and monitoring, allow a comprehensive

**Table 1.** Ultrasound findings in the recipient twin TTTS before and after LC (recipients  $n = 28$ )

| Abnormal findings            | Prenatally present | CHD | Prenatally not present | CHD |
|------------------------------|--------------------|-----|------------------------|-----|
| Hydrops                      | 4                  | 1   | 24                     | 3   |
| MV regurgitation             | 3                  | 1   | 25                     | 3   |
| TV regurgitation             | 9                  | 1   | 19                     | 3   |
| DV absent/reverse            | 10                 | 1   | 18                     | 3   |
| Functional pulmonary atresia | 2                  | 1   | 27                     | 3   |

TTTS – twin-to-twin transfusion syndrome, LC – laser coagulation, CHD – congenital heart defects

and individualised plan for the mode and timing of each pregnancy care and outcome. Twin pregnancies are at increased risk for preterm birth, intrauterine growth restriction (IUGR), and other conditions such as hypertensive disorders and gestational diabetes. Monochorionic twins have additional risks for death and morbidity, primarily because of so called the twin-to-twin transfusion syndrome (TTTS), and for increased congenital abnormalities [1]. TTTS is a serious complication that affects 10-15% of monochorionic multiple pregnancies [2]. Communicating placental vessels on the chorionic plate between the donor and recipient twin are responsible for the imbalance of blood flow dynamics. There is evidence for the superiority of foetoscopic laser ablation-coagulation in solving this haemodynamic disorder.

Survival rates after fetoscopic laser surgery have significantly increased over the last 25 years. High-volume centres report up to 70% double survival rate, and at least one survivor in > 90% of cases. Long-term neurodevelopmental impairment occurs in about 10% of children after laser coagulation (LC) [3].

Congenital heart defects (CHDs) represent the most common human birth defect, having a prevalence at birth of 7-9 per 1000 singleton live births. CHDs are more common in twin pregnancies with a prevalence of 13 per 1000 total births. Monochorionic (MC) twins are at even higher risk (20 per 1000 total births) compared to dichorionic twins (11 per 1000 total births). In MC twins, all types of congenital heart defects have been reported. Furthermore, the development of acquired structural heart disease can be encountered also in association with TTTS [4].

## Material and methods

Our experience of TTTS at Almazov National Medical Research Centre Ministry of Health Russian Federation between April 2019 and March 2020, is related to 28 twin pregnancies in which we performed a careful echocardiographic examination before and after the LC procedure. Our perinatal centre receives the majority of complicated pregnancies from the whole country. Right ventricular outflow tract obstruction was diagnosed or excluded by review of perinatal records, obstetrical ultrasounds, fetal echocardiograms, postnatal echocardiograms, and postnatal clinical assessments. In the cases with RVOTO, the clinical course and postnatal outcome were documented by a review of prenatal and postnatal medical records.

## Results

From our data we observed a series of abnormal prenatal cardiac findings before LC and the postnatal occurrence of structural heart defects in recipients. Donors did not show significant changes in cardiac function, and the Doppler changes were related mainly to the high vascular resistance and occurred in umbilical arteries (high pulsatility index [PI], low diastolic flow, and absent/reversed flow in the umbilical artery). One twin recipient with hydrops and functional pulmonary atresia had the same features at postnatal follow-up; another twin recipient with fetal hydrops, and mitral and tricuspid valve regurgitation presented with moderate pulmonary stenosis postnatally (Table 1).

## Discussion

The increased incidence of CHDs in twins with TTTS can be mainly attributed to the right ventricular outflow tract obstruction (RVOTO) (35/1000 TTTS twin live births vs. 0.5/1000 singleton live births) [5].

Therefore, it is important to understand how the pathophysiological process of TTTS may affect the fetal heart dynamics. It has been demonstrated that in the surface of the twin placenta there can be different types of anastomoses: arterio-venous, which are unidirectional and may cause haemodynamic imbalance, whereas arterio-arterial and the veno-venous anastomoses are bidirectional, and the circulation may remain balanced [6]. In the case of arterio-venous anastomoses, the predominant feature is that blood is mainly going from one fetus to the other. A fetus who is losing its blood volume and becomes hypovolaemic is referred to as the donor. In order to maintain an adequate blood pressure, the twin produces a greater amount of hormonal mediators (renin and angiotensin II), the vascular resistance therefore increases and aggravates the oligo-/anuria as vasopressin and hypoosmolality increase as well. The other fetus, the so-called recipient, becomes hypervolaemic because it receives not only an extra volume of blood but also some of the donor's hormones, which may cause a paradoxical reaction. The recipient has high natriuretic protein and endothelin, which contribute to heart failure. Vasopressin decreases, blood viscosity is high, urine production rises, and there is polyhydramnios [6, 7].

The consequence of an unequal circulatory volume defines the pathophysiology of this condition and determines the physiological responses to the volume imbalance. Moreover, this can lead to functional cardiac changes, usually in the recipient twin. Nevertheless, after the LC procedure, all this is expected to be solved. However, if TTTS progresses, there is the potential for 'acquired' structural congenital heart disease, particularly right ventricular outflow tract obstruction in the recipient and coarctation of the aorta in the donor.

The recipient twin usually has an increased preload. The increase in circulating volume is combined with the donor's hormonal mediators and there is a resulting release of natriuretic peptides, atrial natriuretic protein (ANP), and brain natriuretic protein (BNP), with increasing diuresis and polyhydramnios. Furthermore, the afterload increases as a result of high resis-

tance. There is an increased production of endothelin, which leads to ventricular hypertrophy, hypertension, and inappropriate stimulation of the renin-angiotensin system [6, 7].

The evolution of the functional changes in the recipient twin include ventricular dilatation at the beginning with mild hypertrophy and mild atrioventricular regurgitation [8]; at this time Doppler evaluation in the umbilical artery may still give a normal result. As the disease progresses, there is increasing ventricular thickening and compromised diastolic function. In the ductus venosus, we can observe absent or reversed flow, which is a marker of decreased atrial contraction, and umbilical vein pulsation [9].

As the diastolic function is compromised, the systolic function also deteriorates; there is decreased ventricular short fraction and atrioventricular regurgitation. These alterations usually start in the right side, followed by the left [10]: these modifications may lead to atrioventricular insufficiency and severe ventricular dysfunction, low cardiac output, hydrops, and finally fetal death [11]. The ventricular pressure becomes high before we can observe any outflow obstruction.

Diastolic function in the recipient twin is important for preserving fetal circulation. In the progression of the disease, the ventricular myocardium increases in thickness, therefore reducing the compliance, leading to inadequate relaxation and monophasic ventricular filling instead of the two active and passive phases [12]. Therefore, the so-called myocardial performance index, which describes systolic and diastolic dysfunction, increases.

The myocardial performance index (MPI) is the ratio between the combined isovolumetric times and the ejection time. As the global systolic and diastolic dysfunction worsens, MPI values increase. MPI is a reliable method to understand cardiac function in twins with TTTS using Doppler velocimetry [13, 14].

The twin donor haemodynamics further complicate with decreased preload and increased afterload. The donor rarely manifests cardiac anomalies at echocardiography. Systolic function remains preserved, and there is no effect on valvular function. When the systemic vascular resistance increases, we can find high pulsatility index (PI), low diastolic flow, and absent/reversed flow in the umbilical artery [15]. All of these changes in haemodynamics are aimed at preserving pressure and circulatory redistribution [16, 17].

We usually observe functional cardiac anomalies in the recipient as cardiomyopathy and valvular lesions (pulmonary, tricuspid). In the twin donor there is typically smooth muscle hypertrophy, increased blood pressure, and increased vascular stiffness. Nevertheless, during the progress of TTTS, the twin recipient can manifest acquired cardiac anomalies like right ventricular outflow obstruction or tricuspid valve dysplasia. Some reports show also coarctation of the aorta in the donor twin, but we cannot be sure that it is not congenital and is an underlying cause of the TTTS. All these alterations have long-term consequences [18].

Functional RVOTO may occur as a consequence of right ventricular hypertrophy, reduced RV function, in association

with high systemic pressure, severe tricuspid and pulmonary regurgitation, and an inability of the RV to generate appropriate pressure to open the pulmonary valve.

The ‘acquired’ RV outflow tract obstruction is phenotypically identical to the congenital heart disease (CHD). Pulmonary atresia (PA) or pulmonary stenosis (PS) in the hypoplastic hypertrophic right ventricle [18, 19].

Accurate echocardiographic examination before intervention in TTTS revealed the following: 20% of recipients already had abnormal pulmonary valves before LC treatment, such as atresia or stenosis or regurgitation, and 9–12% showed persistent anomalies requiring surgical treatment at birth despite successful in-utero LC. We still do not know if LC always improves right ventricular function or if early LC reduces the risk of RVOTO [20].

During TTTS, we can observe tricuspid valve anomalies, such as regurgitation, which is one of the haemodynamic anomalies of TTTS, or it can appear after treatment and resolve in a short time. However, it is still unknown if this is a “primary” or “acquired” structural anomaly.

Cardiac anomalies of the twin donor are much less documented – there is a recent report of a series of four donor twins with coarctation and hypoplastic aortic arch [21]. The effect of treatment is unpredictable due to the limited number of cases. Moreover, it is again unknown if the anomalies were “primary” or “acquired” [22].

The purpose of LC is to separate the two twins’ systems of circulation and the discharge of hormonal mediators that cause cardiovascular dysfunction. However, not all cases of RVOTO can be eliminated by performing laser coagulation [10].

The key points are listed in Figure 1.

## Conclusions

Before and after LC an accurate echocardiographic assessment of both twins should always be performed, with particular attention to the presence of the following:

- DV absent/reverse (atrial dysfunction/diminished contractility, stiff non-compliant RV),
- TV, MV regurgitation (dilatation, ventricular hypertrophy, diastolic dysfunction),
- one peak flow ventricular filling (poor compliant and stiff ventricle),
- MPI recipient > MPI donor,
- high gradient of pressure in RV (peak velocity regurgitant jet).

In this way the counselling and the expectations from LC in cases of TTTS will be more accurate and realistic.

### Key points

1. Cardiac malformations are more common in twin pregnancies compared to singleton pregnancies. TTTS further increases the rate.
2. TTTS may contribute to the development of RVOTO, PS, and PA in the recipient and coarctation of the aorta in the donor twin, due to altered blood flow dynamics and hormonal mediators.
3. Cardiac evaluation for both twins (donor and recipient) is warranted.

**Figure 1.** The twin-to-twin transfusion syndrome – key points

## Conflict of interest

The authors declare no conflict of interest.

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